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## Nucleosides, Nucleotides and Nucleic Acids

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### Synthesis and Analysis of Nucleosides Bearing Pyrrolepolyamide Binding to DNA

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## Synthesis and Analysis of Nucleosides Bearing Pyrrolepolyamide Binding to DNA

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### ABSTRACT

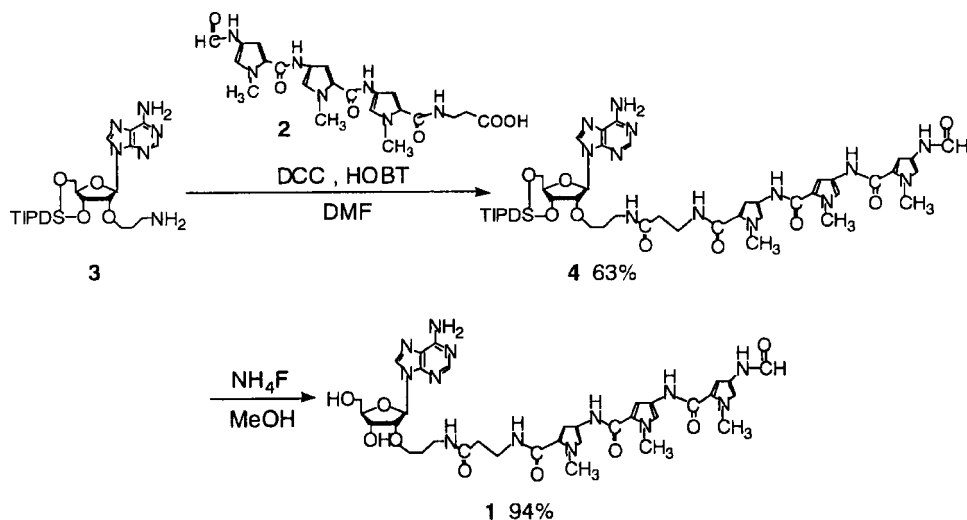
An efficient synthesis of adenosine bearing pyrrolepolyamide **1** was achieved by coupling of **3** with **2**. The CD spectra obtained at several [ligand]/[duplex] ratios allowed verification of the formation complex of the DNA duplex [d(CGCAA-TTGGC)/d(GCCAATTTGCG)] with **1**.

*Key Words:* Nucleoside bearing pyrrolepolyamide; DNA interaction; CD spectra.

Organic compounds which control gene expression is expected to be viable gene therapy medicine. The development of antisense and antigene oligonucleotide as compounds capable of controlling gene expression by recognizing DNA sequence specificity, such as non-natural-oligonucleotides, has been carried out. On the other hand, it was reported that pyrrole- and imidazole-polyamide molecules can recognize sequence-specific DNA.<sup>[1]</sup> On the basis of this background, we expected that nucleosides bearing pyrrolepolyamide would be able to regulate gene expression.

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*Scheme 1.* CD spectra of complex of DNA duplex with 1.

We report here the synthesis of adenosine bearing pyrrolepolyamide (**1**), and analysis of the interaction of DNA duplex [d-(CGCAAATTCG)-d(GCGTTTAAGC)] with **1** by CD spectra.

### SYNTHESIS OF ADENOSINE BEARING PYRROLEPOLYAMIDE

3-(1-Methyl-4-[1-methyl-4-[1-methyl-4-(formylamino)pyrrole-2-carboxamido]pyrrole-2-carboxamido]pyrrole-2-carboxamido) propionic acid (**2**), which is a pyrrolepolyamide bearing carboxyl group at terminus, was prepared from 1-methylpyrrole in nine steps referring to the method of Nishiwaki co-workers<sup>[2]</sup> Waller co-workers<sup>[3]</sup> and Xiao co-workers.<sup>[4]</sup>

2'-O-(3-Aminopropyl)-3',5'-O-TIPDS-adenosine (**3**) was condensed with **2** in the presence of DCC and 1-hydroxybenzotriazole (HOBT) as condensation reagent to give **4** in 63% yield. Finally, **4** was deprotected with ammonium fluoride to give target compound 2'-O-[3-[3-(1-methyl-4-[1-methyl-4-[1-methyl-4-(formylamino)pyrrole-2-carboxamido]pyrrole-2-carboxamido]pyrrole-2-carboxamido)pyrrole-2-carboxamido]propionamido]-propyl}-adenosine (**1**) in 94% yield (Sch. 1).

### CD SPECTRA OF COMPLEX OF DNA DUPLEX WITH 1

Circular Dichroism (CD) spectra was used to investigate binding of **1** to the DNA duplex [d-(CGCAAATTCG)-d(GCGTTTAAGC)]. A CD spectrum for the uncomplexed the DNA duplex indicated the typical B-form conformation.

The addition of Distamycin A of compound **1** results in drastic changes. The CD spectra obtained at several [ligand]/[duplex] ratios allowed verification of the formation complex of the DNA duplex with **1**.

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